REMARKS

Claims 1, 27, 28, 42, 48, 51 and 54-58 were variously rejected under 35 U.S.C. §112, first and second paragraphs. Claims 54-58 were rejected under 35 U.S.C. §103. Claims 1, 51 and 54-58 were objected to.

Claims 1, 42, 48, 51 and 54-58 have been amended herein without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, *inter alia*, throughout the specification. Entrance of this amendment is respectfully requested.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Information Disclosure Statement and Drawings

As requested by the Examiner, copies of the references submitted April 9, 1998 with the Information Disclosure Statement are herewith attached. Also attached are copies of the documents accompanying the references submitted April 9, 1998.

Corrected formal drawings are herewith attached.

Claim objections

Claims 1, 51 and 54-58 were objected to for allegedly containing informalities. The claims have generally been amended in the manner suggested by the Examiner to overcome the objections. Applicants thank the Examiner for helpful suggestions regarding claim language.

With respect to the objection of the phrase "transformed transgenic plant" in claims 56 and 58, Applicants respectfully point out that the full phrase in the claims is "stably transformed, transgenic plant." Since the phase "stably transformed" describes a particular type of transgenic plant, Applicants submit that the phrase is not redundant and this phrase in the claims has not been amended.

In view of the foregoing, Applicants respectfully submit that these objections are moot.

Rejections under 35 U.S.C. §112, first paragraph

Written Description

Claims 1, 27, 28, 42, 48, 51 and 54-58 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this ground for rejection.

The Examiner states that Applicants do not "describe the composition or structure of any microbial DNA sequences encoding endo-glucanase, required for production of the claimed expression cassettes and transgenic plants, and to practice the claimed methods." Office Action, page 4. In support of the rejection, the Examiner cites *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) and quotes therefrom that "naming a type of material

generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material."

Applicants respectfully traverse this rejection and submit that the cited court decision is not pertinent to the facts of the present invention.

The specification lists examples of endo-glucanases, such as endo-1, 3-β-glucanase (E.C. 3.2.1.6) and endo-1, 4-β-glucanase (E.C. 3.2.1.4), for example, at page 6, lines 31-32, as types of endo-glucanases for use in the claimed invention. Although not explicitly presented in the specification, nucleic acid sequences encoding microbial endo-glucanases were well known in the art at the time the application was filed. Applicants have herewith attached, as Appendix B, a list of example publications which describe nucleic acid sequences encoding microbial endo-glucanases. The publications on this list include examples of endo-glucanase encoding sequences from a variety of microbial species. All of these references were published prior to the priority date of the present invention. At the Examiner's request, Applicants will be happy to supply a copy of the listed references. Applicants note that Baird et al. (March, 1990), cited by the Examiner in the current Office Action and addressed below, presents nucleic acid sequences encoding of a *Bacillus polymyxa* endo-glucanase and, in turn, further cites a number of references describing additional microbial endo-glucanase sequences.

Thus, contrary to the Examiner's selected quote from *University of California v. Eli Lilly and Co,* the claimed invention does not merely name a type of material generally know to exist. Nucleic acid sequences encoding microbial endo-glucanases were well known in the art at the time of filing. The written description requirement "may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure" and compliance with the requirement "is essentially a fact-based inquiry that will 'necessarily vary

depending on the nature of the invention claimed.'" See *Amgen, Inc. v. Hoechst Marion Roussel, Inc. and Transkaryotic Therapies, Inc.*, USPQ 65 USPQ2d 1385 (Fed. Cir. 2003); *Enzo Biochem, Inc. v Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). Applicants respectfully submit that the specification in combination with that known in the art adequately describes possession of the claimed genus to one skilled in the art.

In view of the foregoing, Applicants respectfully submit that the written description requirement has been met.

Enablement

Claims 1, 27, 28, 42, 48, 51 and 54-58 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

The claimed invention is directed to a method of modifying polysaccharide/saccharide composition of a plant or plant organ by growing a transgenic plant containing nucleotide sequence encoding a microbial endo-glucanase operably linked to a regulatory or leader sequence under conditions where the glucanase is expressed. The claimed invention is also directed to a recombinant DNA expression cassette for use in the method and to transgenic plants generated by the method or with the expression cassette.

Representative glucanases are set forth in the specification on page 6, starting at line 20, including endo-glucanases. As presented herein, nucleic acid sequences encoding microbial endo-glucanases were known in the art at the time of filing. The delivery of the enzymes to a desired site merely involves the selection of a known regulatory element or targeting leader. The elements for doing this are known and described in the specification. Useful targeting leader

sequences are set forth starting at line 25 on page 10. Useful regulatory sequences are set forth starting on line 24 of page 9. Suitable plants are illustrated on page 8 starting at line 25.

The examples, especially Examples 3-5, 7-8, and 11-12 illustrate the operation of the invention in a variety of plants, e g. potato, tomato, tobacco, using various approaches, e.g. agrobacterium, tuber-specific expression construct, and enzymatic modification of polysaccharide/saccharide at various sites, e.g. leaves, roots and fruit. The specific types of glucanase used is not critical and their selection is based on the desired end. The activity of endo-glucanases and techniques to assess endo-glucanase activity are well known in the art.

The specification, including the examples, illustrates the operation of the invention. Following these teachings using conventional materials is not seen to involve undue experimentation. The stated object is merely to modify polysaccharide/saccharide composition of the plant or plant organ. The nature of the modification, e.g. presence of oligo- and/or monosaccharides, is described as is its monitoring using conventional assays.

The Examiner asserts that the "state of the art for isolation of cDNA or genomic clones with a defined functionality is highly unpredictable" and "undue trial and error experimentation would be required to screen through the vast number of cDNA and genomic clones from any and all microbial organisms, to identify those that encode endo-glucanase and can be used in the claimed method." Office Action, page 7. Applicants respectfully disagree with this assertion.

As outlined above, nucleic acid sequences encoding endo-glucanases from a variety of microbial species were known in the art at the time of filing. In addition, according to the sworn testimony of Dr. Pen, "identification, characterization, and testing of nucleotide sequences (i.e., microbial endo-glucanases) encompassed by these claims could readily be carried out by a person skilled in the art using known techniques." Pen Declaration, submitted August 1, 2000,

paragraph 2. Baird et al., for example, describes identifying, characterizing and expressing endo-glucanase encoding sequences from two species of *Bacillus*.

Thus, to make and/or use the claimed invention, a skilled artisan could use one of many known microbial endo-glucanase encoding sequences or could readily identify and use a desired microbial endo-glucanase encoding sequence.

The Examiner also asserts that the "state of the art for modification of phenotype, including sugar and carbohydrate production, in transgenic plants is highly unpredictable." Office Action, page 7. In support of this statement, the Examiner cites Harpster et al. (2002, "Harpster") and Carvalho et al. (1992, "Carvalho"), two references not concerned with microbial source genes. With regard to Harpster, the Examiner states that "overexpression of a pepper endo-glucanase nucleic acid in tomato did not have the anticipated effect on xyloglucan depolymerization or fruit softening." Applicants respectfully disagree with this assertion regarding the state of the art.

As noted, Harpster is not concerned with microbial source polynucleotides and thus is not directly pertinent to the claimed invention. However, "between one-quarter and over one-third of non-xyloglucan matrix glycans were lost from the 24% KOH-soluble extract" of the transgenic plants in Harpster. See, for example, page 364 and Figure 5A. In addition, Harpster reported a loss of other higher molecular weight matrix glycans in the transgenic plants expressing the pepper endo-glucanase. See, for example, page 366 and Figure 6. Thus, although depolymerization of the particular glycan xyloglucan was not observed, the polysaccharide/saccharide composition of the transgenic plants in Harpster was modified by the expression of the pepper endo-glucanase.

Carvalho also describes the use of plant-derived genes for transformation to plants, in this case within the same genus. Given the close relationship of the plant from which the gene was obtained and the plant into which the gene has been transformed, it could be expected that there is interference with the endogenous gene already present in the host plant. However, Carvalho observes a transgene "gene silencing" phenomenon in only one of five transgenic plant lines, and only in plants homozygous for the transgene derived from that one particular line. Thus, the great majority of the transgenic plant lines reported in Carvalho express the transgene apparently as expected. In addition, gene silencing as reported in Carvalho was not reported in Harpster nor in the examples of the specification. Thus, Applicants submit that the cited references when taken in their entirety do not support the alleged state of high unpredictability with regard to the claimed invention.

Applicants respectfully submit that the provided references do not provide acceptable documentation or sound scientific reasoning to support any doubt the teachings of the specification. See, for example, *In re Marzocchi*, 439 F2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). Unless such documentation and/or scientific reasoning are adduced, the statements made in the specification are to be taken at face value.

Respectfully, then, Applicants believe that the Office has failed to establish such a "high degree of unpredictability" that the statements of the application should be doubted and the working examples considered unrepresentative. Applicants respectfully submit that the specification provides adequate guidance to one skilled in the art to make and/or use the claimed invention. Accordingly, the pending claims are in compliance with the enablement requirements.

In sum, Applicants submit that the pending claims fall within the subject matter that is enabled and described by the specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

Claims 1, 27, 28, 42, 48, 51 and 54-58 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

Although Applicants believe that the claims were sufficiently definite when considered in view of the specification and the understanding of those of skill in the art, Applicants have attempted to respond to the concerns of the Examiner in order to enhance clarity and to facilitate disposition of the present case. Applicants of course welcome any additional suggestions the Examiner may have and would appreciate the opportunity to discuss the claims with the Examiner after she has had an opportunity to review this Amendment and Response in order to ensure that the case can be placed into condition for allowance.

With regard to claim 1 at line 1, the Examiner states that "the phrase "polysaccharide/saccharide material" is indefinite and that it "is not clear what components of the composition are modified and how they are modified." Office Action, pages 8-9. Applicants respectfully point out that the claimed method is directed to modifying the polysaccharide/saccharide composition of a plant or plant organ through expression of a microbial endo-glucanase, a polysaccharide degrading enzyme, in the plant. Thus, the polysaccharide/saccharide content of the plant or plant organ is altered.

With regard to claim 1 at line 12, the Examiner states that the phrase ""the polysaccharide/saccharide material" is indefinite" and that it "is not clear what is intended, *i.e.* what components of cellular compartments or organelles." Office Action, page 9. Applicants respectfully point out that the claimed method is directed to modifying the polysaccharide/saccharide composition of a plant or plant organ and that the leader sequence targets the expressed endo-glucanase to polysaccharide/saccharide material in a desired cellular compartment or organelle.

With regard to claim 42, the Examiner suggests that the term "contains" be changed to "comprises" to clarify that open claim language is intended. Applicants have retained the term "contains" and respectfully point out that the transitional term "comprising" is synonymous with "containing" and both terms are inclusive or open-ended. M.P.E.P. §2111.03.

With regard to claim 42, the Examiner states that ""a second microbial enzyme" does not make sense because "a first microbial enzyme" is not previously recited." Office Action, page 9. Applicants respectfully point out that claim 1 describes an expressed microbial endo-glucanase and, for the purposes of claim 42, the expressed glucanase of claim 1 is the first microbial enzyme.

The Examiner states that claim 58 is improperly dependent from claim 1. Applicants respectfully point out that the method of claim 1 includes the optional use of a leader sequence that targets the expressed endo-glucanase to polysaccharide/saccharide material contained in a cellular compartment or organelle of the transgenic plant. Claim 58 is directed to a transgenic plant or plant organ, made by the method of claim 1, with endo-glucanase modified material contained in a cellular compartment or organelle. Thus, Applicants respectfully submit that claim 58 is properly dependent from claim 1.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. §103

Claims 54-58 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Cornelissen et al. (U.S. Pat. No. 6,066,491; effective filing date 1/29/91) or Cornelissen et al. (EP 440,304; published 8/7/91), either in view of Baird et al. (*J. Bacteriol.* 172:1576-1586, March, 1990, "Baird"). Applicants respectfully traverse this rejection.

Applicants respectfully submit that both the Cornelissen et al. references on which the rejection is based are not properly cited prior art under 35 U.S.C. §102. The instant application claims priority under 35 U.S.C. §119 to the application EPO 90202438.4 filed September 13, 1990. Thus, the Cornelissen et al. references are not available as prior art under any 35 U.S.C. §102 section and accordingly, not available for citation under §103.

Baird describes cloning and sequence analysis of a *Bacillus polymyxa* endo-glucanase gene and demonstrated sequence similarity between it and endo-glucanase genes from *Bacillus circulans* and from *Clostridium thermocellum*. Baird neither describes nor suggests the generation of DNA expression cassettes for expression of the microbial endo-glucanase in transgenic plants. Baird does not describe or suggest a transgenic plant containing a nucleotide sequence encoding a microbial endo-glucanase. Further, Baird provides no motivation for one skilled in the art to modify the teachings therein to arrive at the presently claimed invention.

Accordingly, Baird does not support *prima facie* obviousness with regard to the claimed invention. Applicants respectfully submit that a *prima facie* case of obviousness has not been established.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

CONCLUSION

Applicants have, by way of the amendments and remarks presented herein, addressed all issues that were raised in the outstanding Office Action. Applicants respectfully contend that this Amendment and Response has overcome the rejections and that the pending claims are in condition for allowance. If it is determined that a telephone conversation would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 261922003302.

Respectfully submitted,

Dated: May 12, 2003

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EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please enter the following amendments without prejudice or disclaimer.

In the Claims:

1. (Five times amended) A method for modifying the polysaccharide/saccharide composition of a plant or plant organ, wherein said method comprises growing a [transformed] transgenic plant containing a vector or recombinant expression construct containing a nucleotide sequence encoding a microbial endo-glucanase operably linked to a regulatory or leader sequence under conditions wherein said glucanase is expressed and the [carbohydrate] polysaccharide/saccharide composition of said plant or plant organ is modified by the expressed glucanase and said regulatory sequence is selected from the group consisting of

a) a regulatory sequence that directs expression of said [enzyme-encoding] microbial endo-glucanase-encoding nucleotide sequence at a selected stage of development or maturity of the transgenic plant or plant organ;

b) a regulatory sequence comprising a [35S] CaMV 35S promoter; and

c) a regulatory sequence that directs tissue-specific expression of said [enzyme-encoding] microbial endo-glucanase-encoding nucleotide sequence in a plant; and

wherein said leader sequence targets the expressed endo-glucanase to [the] polysaccharide/saccharide material contained in a cellular compartment or organelle.

42. (Twice Amended) The method of claim 1, wherein said transgenic plant further contains at least one expression cassette which contains a nucleotide sequence encoding a second microbial enzyme that acts upon degradation products resulting from the action of the [first enzyme] expressed glucanase.

48. (Twice Amended) The method of claim 42, wherein the second microbial enzyme is selected from the group consisting of a maltase, an α-dextrinase, an α-1,6-glucosidase, a glucose isomerase and an invertase.

51. (Amended) The method of claim 1, [further characterized in that] wherein said transgenic plant is selected from the group consisting of tomato, potato, corn, cassava, carrot, lettuce, strawberry and tobacco.

54. (Four times amended) A recombinant DNA expression cassette comprising a regulatory sequence operably linked to a nucleotide sequence encoding [an] a microbial endo-glucanase which regulatory sequence is selected from the group consisting of

a) a regulatory sequence that directs expression of said [enzyme-encoding] microbial endo-glucanase-encoding nucleotide sequence at a selected stage of development or maturity of the transgenic plant or plant organ;

b) a regulatory sequence comprising a [35S] CaMV 35S promoter; and

c) a regulatory sequence that directs tissue-specific expression of said enzyme-encoding nucleotide sequence in a plant.

55. (Amended) A vector comprising [an] the expression cassette according to claim 54.

56. (Thrice amended) A stably transformed, transgenic plant, [characterized in that] wherein said plant contains a stably integrated [gene] nucleotide sequence comprising a regulatory sequence operably linked to a sequence encoding a microbial endo-glucanase resulting from the introduction of [an] the expression cassette according to claim 54.

57. (Amended) A bacterial strain [characterized in that] wherein said bacterial strain contains a vector according to claim 55.

58. (Four times amended) A stably transformed, transgenic plant or plant organ, [characterized in that] wherein said plant or plant organ contains [a] endo-glucanase modified polysaccharide/saccharide [composition] material contained in a cellular compartment or organelle, said plant or plant organ being made by the method of claim 1.

EXHIBIT B

List of example publications including microbial endo-glucanase nucleic acid sequences.

Murphy et al. (1984) "The DNA sequence of the gene and genetic control sites for the excreted B. subtilis enzyme beta-glucanase." *Nucleic Acids Res.* 12:5355-5367.

Beguin et al. (1985) "Sequence of a cellulase gene of the thermophilic bacterium Clostridium thermocellum." *J. Bacteriol.* 162:102-105.

Fukumori et al. (1986) "Molecular cloning and nucleotide sequence of the alkaline cellulase gene from the alkalophilic Bacillus sp. strain 1139" *J. Gen. Microbiol.* 132:2329-2335.

Fukumori et al. (1986) "Nucleotide sequences of two cellulase genes from alkalophilic Bacillus sp. strain N-4 and their strong homology." *J. Bacteriol.* 168:479-485.

Joliff et al. (1986) "Nucleotide sequence of the cellulase gene celD encoding endoglucanase D of Clostridium thermocellum." *Nucleic Acids Res.* 14:8605-8613.

Pentilla et al. (1986) "Homology between cellulase genes of Trichoderma reesei: complete nucleotide sequence of the endoglucanase I gene." *Gene* 45:253-263.

Wong et al. (1986) "Characterization and structure of an endoglucanase gene cenA of Cellulomonas fimi." *Gene* 44:315-324.

Robson et al. (1987) "Endo-beta-1,4-glucanase gene of Bacillus subtilis DLG." *J. Bacteriol.* 169:2017-2025.

Guiseppi et al. (1988) "Homology between endoglucanase Z of Erwinia chrysanthemi and endoglucanases of Bacillus subtilis and alkalophilic Bacillus." *Mol. Microbiol.* 2:159-164.

Hall et al. (1988) "The nucleotide sequence of a carboxymethylcellulase gene from Pseudomonas fluorescens subsp. cellulosa." *Mol. Gen. Genet.* 213:112-117.